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CLAIM

1. A method, for preparing a natural humanized antibody, which comprises conducting a homology search for the FR of a primary design antibody and selecting a natural human FR retaining the artificial amino acid residues contained in the FR of the primary design antibody and having a homology therewith.

2. The method of preparing a natural humanized antibody according to claim 1, which comprises conducting a homology search for the FR of a primary design antibody, selecting a natural human FR retaining the artificial amino acid residues contained in the FR of the primary design antibody and having a homology therewith, and replacing one or a plurality of different amino acid residues between the FR of the primary design antibody and the selected natural human FR.

3. The method of preparation according to claim 1 or 2, wherein the primary design antibody comprises CDRs derived from a first animal species, and FRs derived from a second animal species and having artificial amino acid residues.

4. The method of preparation according to claim 3, wherein the first animal species is rat and the second animal species is human.

5. The method of preparation according to ^{Claim 1} ~~any of claims 1 to 4~~, wherein the artificial amino acid residues are derived from the FR of non-human antibody.

6. A natural humanized antibody obtained by a method of preparation according to ^{Claim 1} ~~any of the claims 1 to~~

7. A natural humanized antibody containing CDR

derived from a first animal species and the FR derived from a second animal species, characterized in that said FR comprises an amino acid sequence having amino acid residue different from the FR used for CDR-grafting by one or a plurality of amino acid residues and that said FR has been replaced with an FR derived from a second

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animal species and having the same amino acid residues as said different amino acid residue at the same positions.

- 5 8. The natural humanized antibody according to claim 7, wherein the first animal species is rat and the second animal species is human.

a 9. DNA encoding the natural humanized antibody according to ^{Claim 6} ~~any of claims 6 to 8~~.

- 10 10. An expression vector comprising the DNA according to claim 9.
- 10 11. A host comprising the DNA according to claim 10.

- 15 12. A method of preparing a natural humanized antibody, which comprises culturing the cells into which an expression vector comprising the DNA according to claim 9 has been introduced and recovering the desired natural humanized antibody from the culture of said cells.

13. A pharmaceutical composition comprising a natural humanized antibody.

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